

130. (New) The kit of claim 129, wherein said microchip further comprises an injection channel formed in said substrate, and disposed for fluid communication with said electroseparation channel.

131. (New) The kit of claim 130, wherein said injection and electroseparation channels intersect one another.

132. (New) The kit of claim 130, wherein said microchip further comprises a loading reservoir formed in said substrate, and disposed for fluid communication with said injection channel.

133. (New) The kit of claim 129, further comprising a denaturing electrophoretic medium.

134. (New) The kit of claim 129, wherein said microchip is disposable.

#### REMARKS

Following entry of the above amendments and new claims, claims 54, 57-62, and 64-71, and 75-134 will be pending in this application and are presented for examination.

#### Claim Amendments

The claims are amended to substitute the abbreviation PNA for peptide nucleic acid. Basis for this amendment can be found throughout the specification and in particular on page 3, line 12, and on page 9, line 3.

The independent claims 54, 57, 58, 71 and 115 are also amended to clarify that the peptide nucleic acid probes are mobilizable at least within the separation zone. Support for this amendment can be found throughout the specification and in particular on page 11, lines 9-24, on page 13, lines 17-26, on page 14, lines 15-24, and in the examples and the figures.

The independent claims 54, 57, 58, 71 and 115 are also amended to clarify that the peptide nucleic acid probe(s) is (are) disposed within the apparatus. Support for this amendment can be found throughout the specification and in particular from page 27, line 25 to page 28, line 3.

The independent claims 54, 57, 58, 71 and 115 are amended to recite an electrophoretic separation channel or zone within a capillary channel. Support for this amendment can be found throughout the specification and in particular on page 5, lines 9-10, in figures 12 to 15 and accompanying description on pages 27 to 30, and in examples 5 to 9.

Claim 59 is amended to recite an electrophoretic sieving medium. Support for this amendment can be found throughout the specification and in particular on page 5, lines 15, from page 13, line 27 to page 14, line 27.

New claims 119 to 128 are directed to methods of conducting electrophoresis of DNA sample using labeled PNA probes. Support for this amendment can be found throughout the specification and in particular on pages 4 and 5, on pages 12 to 15, and in examples 5 to 9.

New claims 129 to 134 are directed to a kit for conducting electrophoresis with a capillary microchip and a labeled PNA probe. Support for this amendment can be found throughout the specification and in particular on page 30, lines 16-28, and on page 35, line 6.

**Rejection of Claims under 35 U.S.C. §112, Second Paragraph**

Claims 54, 57-62, 64-71, and 75-118 are rejected under 35 U.S.C. §112, second paragraph as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter applicants regard as the invention.

In particular, the examiner requests clarification of the relationship between the apparatus and the peptide nucleic acid probe (PNA probe). Applicants believe that such clarification is not required as the claim language clearly recites an apparatus comprising a PNA probe, and as such, sets forth the PNA probe as a component of the apparatus. Applicants further believe that a specific relationship between the PNA probe and the remaining components of the apparatus is also not required. Such specific relationship is purposefully and legitimately not set forth to provide adequate breadth to the claim to cover the apparatus before, during, and after its use. Indeed, the PNA probe is a mobilizable component within the apparatus, and thus the PNA probe may be located in various components of the apparatus at various stages of its use. The specification clearly supports the breadth of the claims as it describes the apparatus with the PNA probe in the various zones:

- in the sample introduction zone (for example in page 27, line 27 to page 28, line 16; and the figures),
- in the incubation zone (for example in page 13, lines 12-16; page 27, line 27 to page 28, line 16; and the figures),
- in the separation channel (for example in page 13, lines 17-26; page 24, lines 13-14; page 27, lines 4-11; page 28, lines 14-16; and the figures),
- or in the detection zone (for example in page 15, lines 14-20; page 24, line 14; page 27, lines 4-11; and the figures).

Breadth should not be equated to indefiniteness. *In re Miller*, 441 F.2d 689, 169 USPQ 597 (CCPA 1971); MPEP §2173.04. Applicants have nonetheless amended the claims where appropriate to specify that the PNA probe is disposed within the apparatus and is mobilizable at least within the separation zone.

Also, the examiner requests clarification of the communicative relationship between the various zones. Applicants believe that such clarification is also not required. Again, specific relationships are purposefully and legitimately not set forth to provide adequate breadth to the claim to cover the various embodiments of the apparatus. What is required for proper operation of the device, and is properly set forth in the claims, is that the various zones be in communication with each other to permit motion of the sample and reagents from one zone to the other. The specification clearly supports the breadth of the claims as it describes apparatus with zones in direct or indirect communication with each other. For example, in Figure 13, a reservoir (26)—which depending on the polarity of the voltage may be used as an incubation zone (A) or a waste reservoir (B)—is in communication with both the sample introduction zone (24) and the separation zone (20); yet in figures 12 and 14, these zones are connected by channels. Applicants respectfully submit that here again, breadth should not be equated to indefiniteness and that the rejection should be withdrawn.

#### **Rejection of Claims Under 35 USC § 102(e)**

Claim 54, 57, 86, 89, 92-94, 107-110, 115, and 116 are rejected under 35 U.S.C. §102(e) as being allegedly anticipated by Weininger et al. Applicants respectfully submit that the claims

are patentable over the cited art. Nonetheless, Applicants have amended the claims as suggested by the examiner.

The examiner's reliance on Weininger is based on Weininger's use of the abbreviation PNA to designate traditional nucleic acid probes (with polydeoxyribophosphoric backbone) and that allegedly, the instant application does not provide a succinct definition of a PNA as a peptide nucleic acid. Applicants have amended the claims to spell out the abbreviation as suggested by the examiner. Applicants further points to the specification where a definition of PNA is set forth on at least two occurrences: on page 3, line 12, i.e., "Peptide Nucleic Acids or PNAs have been determined to be useful probe substitutes;" and on page 9, lines 3-4, i.e., "The term PNA (peptide nucleic acid), as used herein, refers to a DNA mimic with a neutral polyamide backbone on which the nucleobases are attached...." (Emphasis added). Accordingly, Applicants respectfully request that this rejection be withdrawn.

#### **Rejection of Claims Under 35 USC § 103**

Claims 54, 57-59, 61, 64-71, 75-86, 88-94, and 96-118 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over US5,726,026 to Wilding et al. ("Wilding") in view of Summerton. Without acquiescing into the examiner's bases for rejection, Applicants have amended the claims to clarify that the PNA probes of the invention are mobilizable at least within the separation zone of the apparatus, and to further define the separation zone as an electrophoretic channel and the sieving medium as electrophoretic. Applicants respectfully submit that the amended claims and the new claims are patentable over the cited art as outlined below.

Wilding does not teach apparatuses wherein a labeled PNA probe is mobilizable through a separation zone, let alone a labeled PNA probe. Wilding rather teaches away in at least three respects. In a first aspect, the devices of Wilding do not use mobilizable probing reagents to conduct analytical assays. Rather, in Wilding devices, the sample is directly transferred from an introduction zone—or reaction chamber for conducting PCR—to a detection zone where the probing reagent resides (col. 4, lines 33-41).

In a second aspect, the devices of Wilding use separation zones to separate particulate components from the sample (Wilding in col. 3, lines 46-50, col. 5, lines 5-15, and col. 16, lines

28-30). The separation zone of Wilding does not appear to permit electrophoretic sieving or mobilization of a probe therethrough.

In a third aspect, Wilding teaches away from conducting electrophoresis within the devices. At column 20, lines 49-52, Wilding specifically discloses that "the amplified polynucleotide may be also detected outside the devices using ...electrophoresis." (Emphasis added).

Summerton is not properly combinable with Wilding and does not cure the defects of Wilding. To the extent that Wilding is combined with Summerton to render unpatentable the present claims directed to particulate probes, this combination is improper. As shown above, Wilding teaches away from apparatuses of the presently claimed invention as Wilding devices describes separation zone that eliminates particulate components. Thus a skilled artisan would not have the motivation to combine the particulate probes of Summerton with the devices of Wilding with an expectation that the probes would be mobilizable through the separation zone of Wilding.

To the extent that Wilding is combined with Summerton to render unpatentable the present claims directed to peptide nucleic acid labeled with other detectable moieties, Summerton fails to cure the defects of Wilding. Summerton does not teach the use of its probes for polynucleotide identification through electrophoresis. Also, as maintained before, Summerton does not teach DNA mimic probe labeled with non-particulate detectable moieties. Rather the detectable moieties of Summerton are molecules that bind to the phosphoric groups of the DNA/RNA samples—not the DNA mimic probe. Thus even if combined, these references still do not teach or suggest the invention as claimed.

Thus Applicants submit that the amended and new claims are patentable over the cited art and respectfully request that this rejection be withdrawn.

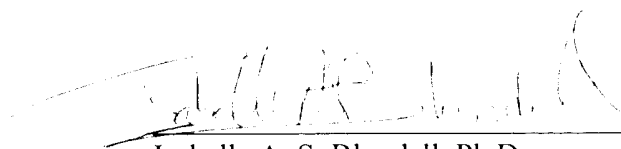
### **CONCLUSION**

Applicants respectfully submit that this Amendment places the pending claims in condition for allowance. The Examiner is cordially invited to contact the undersigned by any means indicated below to promote expeditious resolution of this case.

Respectfully submitted,

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Reg. No. 43,321

Direct Tel.: (617) 248-7634  
Direct Fax: (617) 790-0034  
E-mail: blundell@tth.com



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Isabelle A. S. Blundell, Ph.D.  
Attorney for Applicant(s)  
Testa, Hurwitz, & Thibault, LLP  
High Street Tower  
125 High Street  
Boston, Massachusetts 02110

54. (Twice Amended) An apparatus comprising:

- a) a sample introduction zone;
- b) at least one ~~PNA~~ peptide nucleic acid probe associated with a particle;  
and
- c) an electrophoretic separation zone~~channel~~ in communication with said introduction zone;

wherein the peptide nucleic acid probe is disposed within the apparatus and is mobilizable at least within the separation channel.

57. (Twice Amended) An apparatus comprising:

- a) a sample introduction zone;
- b) an electrophoretic separation zone~~channel~~ in communication with said introduction zone;
- c) at least one ~~PNA~~ peptide nucleic acid probe labeled with a detectable moiety, said ~~PNA~~ peptide nucleic acid probe disposed within the apparatus upstream of said separation zone~~channel~~ and being mobilizable at least within the separation channel; and
- d) a sample incubation zone disposed in communication with the sample introduction zone and in communication with the separation ~~zone~~channel.

58. (Twice Amended) A microchip apparatus comprising a plurality of capillary channels, each said capillary channel further comprising:

- a) a sample introduction zone;
- b) an electrophoretic separation zone in communication with said introduction zone;

- c) \_\_\_\_\_ at least one ~~PNA~~ peptide nucleic acid probe labeled with a detectable moiety, said ~~PNA~~ peptide nucleic acid probe being mobilizable at least within the separation zone and disposed within the apparatus to mix upstream of a the separation zone with a sample introduced in each said introduction zone, said sample comprising at least one double stranded polynucleotide, said at least one ~~PNA~~ peptide nucleic acid probe having a sequence complementary to a selected target sequence suspected to be present in said at least one double stranded polynucleotide;
- e)d) \_\_\_\_\_ a nucleic acid/nucleic acid denaturing reagent permitting the formation of a ~~PNA~~ peptide nucleic acid probe/nucleic acid complex when said selected target sequence is present;
- d)e) \_\_\_\_\_ a detection zone; and
- e)f) \_\_\_\_\_ said separation zone in communication with said introduction zone and said detection zone.
59. (Amended) The microchip apparatus of claim 58 wherein the separation zone of at least one of said capillary channel comprises an electrophoretic sieving medium.
64. (Twice Amended) The microchip apparatus of claim 58 wherein at least one of said at least one ~~PNA~~ peptide nucleic acid probe comprises a charge-modifying moiety.
66. (Twice Amended) The microchip apparatus of claim 58 wherein said at least one ~~PNA~~ peptide nucleic acid probe is associated with a particle.
71. (Amended) A microchip apparatus comprising a plurality of capillary channels, wherein each of said capillary channels further comprises:
- a) a sample introduction zone;

b) an electrophoretic separation zone in communication with said introduction zone;

b)c) at least one ~~PNA~~ peptide nucleic acid probe labeled with a detectable moiety,  
said ~~PNA~~ peptide nucleic acid probe disposed within the apparatus upstream of the  
separation zone and being mobilizable at least within the separation zone; and

e)d) a detection zone; wherein said separation zone is in communication with said  
introduction zone and said detection zone.

83. (Amended) The microchip apparatus of claim 58 wherein the ~~PNA~~ peptide  
nucleic acid probe is modified with the detectable moiety.

84. (Amended) The microchip apparatus of claim 58 wherein the detectable moiety is  
bound to the ~~PNA~~ peptide nucleic acid probe.

85. (Amended) The microchip apparatus of claim 58 wherein the detectable moiety is  
associated to the ~~PNA~~ peptide nucleic acid probe.

86. (Amended) The apparatus of claim 54 wherein the separation ~~zone~~channel  
comprises an electrophoretic sieving medium.

90. (Amended) The apparatus of claim 54 wherein said at least one ~~PNA~~ peptide  
nucleic acid probe further comprises a charge-modifying moiety.

92. (Amended) The apparatus of claim 54 further comprising a sample incubation  
zone disposed in communication with said sample introduction zone and said separation  
~~zone~~channel.

93. (Amended) The apparatus of claim 54 further comprising a sample detection zone  
disposed in communication with said separation ~~zone~~channel.

94. (Amended) The apparatus of claim 57 wherein the separation ~~zone~~channel  
comprises an electrophoretic sieving medium.

98. (Amended) The apparatus of claim 57 wherein said at least one ~~PNA~~ peptide nucleic acid probe comprises a charge-modifying moiety.

107. (Amended) The apparatus of claim 57 wherein the ~~PNA~~ peptide nucleic acid probe is modified with the detectable moiety.

108. (Amended) The apparatus of claim 57 wherein the detectable moiety is bound to the ~~PNA~~ peptide nucleic acid probe.

109. (Amended) The apparatus of claim 57 wherein the detectable moiety is associated to the ~~PNA~~ peptide nucleic acid probe.

110. The apparatus of claim 57 further comprising a sample detection zone disposed in communication with said separation ~~zone~~ channel.

111. (Amended) The microchip apparatus of claim 71 wherein the detectable moiety is bound to the ~~PNA~~ peptide nucleic acid probe.

112. (Amended) The microchip apparatus of claim 71 wherein the ~~PNA~~ peptide nucleic acid probe is bound to biotin.

113. (Amended) The microchip apparatus of claim 71 wherein the ~~PNA~~ peptide nucleic acid probe is bound to fluorescein.

114. (Amended) The microchip apparatus of claim 71 wherein the ~~PNA~~ peptide nucleic acid probe is modified with the detectable moiety.

115. (Amended) An apparatus comprising:

a. a sample introduction zone;

b. an electrophoretic separation ~~zone~~ channel in communication with said introduction zone;

c. at least one ~~PNA~~ peptide nucleic acid probe modified with a label, said label comprising a detectable moiety, said ~~PNA~~ peptide nucleic acid probe disposed within said apparatus upstream of said separation ~~zone~~channel and being mobilizable at least within the separation channel; and

d. a sample incubation zone disposed in communication with the sample introduction zone and in communication with the separation ~~zone~~channel.

116. (Amended) The apparatus of claim 115 wherein the detectable moiety is bound to the ~~PNA~~ peptide nucleic acid probe.

117. (Amended) The apparatus of claim 115 wherein the ~~PNA~~ peptide nucleic acid probe is bound to biotin.

118. (Amended) The apparatus of claim 115 wherein the ~~PNA~~ peptide nucleic acid probe is bound to fluorescein.

119. (New) A method for separating DNA-containing samples, comprising:

(a) providing a sample-separation device including an injection channel and an electroseparation channel, with said injection channel being disposed for fluid communication with said electroseparation channel;

(b) placing an electrophoretic medium in said electroseparation channel;

(c) mixing (i) a peptide nucleic acid (PNA) probe labeled with a detectable moiety and a (ii) double-stranded-DNA-containing sample under conditions permitting PNA-DNA hybrids to form, but disfavoring DNA-DNA hybrids;

(d) introducing the mixture from step (c) into said injection channel;

(e) applying an electrical potential along at least one of said channels sufficient to cause PNA-DNA hybrids to migrate into and along said separation channel; and

(f) detecting for said detectable moiety.

120. (New) The method of claim 119, wherein said injection and electroseparation channels intersect one another.

121. (New) The method of claim 120, wherein said sample-separation device further comprises a reservoir, with said reservoir being disposed for fluid communication with said injection channel.

122 (New) The method of claim 121, wherein said injection channel, said electroseparation channel, and said reservoir are formed in a microchip.

123. (New) A method for separating samples, comprising:

(a) providing an electroseparation channel;

(b) placing an electrophoretic medium in said electroseparation channel;

(c) mixing (i) a sample comprised of target DNA strands and DNA strands complementary to said target DNA strands, and (ii) a peptide nucleic acid (PNA) probe labeled with a detectable moiety, said PNA probe having a sequence complementary to at least a portion of said target DNA strands, whereby PNA-DNA hybrids are formed;

(d) introducing said PNA-DNA hybrids into said electroseparation channel;

(e) applying an electrical potential along said electroseparation channel sufficient to cause PNA-DNA hybrids to migrate along said electroseparation channel; and

(f) detecting for said PNA-DNA hybrids.

124. (New) The method of claim 123, wherein said mixing is carried out under denaturing conditions, disfavoring DNA-DNA hybrids.

125. (New) A method for separating samples, comprising:

(a) providing a sample comprised of double-stranded DNA;

\_\_\_\_\_ (b) denaturing said double-stranded DNA to form single-stranded DNA comprising target DNA strands and DNA strands complementary to said target DNA strands;

\_\_\_\_\_ (c) incubating the target DNA strands and DNA strands complementary to the target DNA strands with a a peptide nucleic acid (PNA) probe labeled with a detectable moiety, said PNA probe having a sequence complementary to at least a portion of said target DNA strands, whereby DNA-PNA hybrids are formed;

\_\_\_\_\_ (d) electrophoresing said DNA-PNA hybrids; and

\_\_\_\_\_ (e) detecting for said PNA-DNA hybrids.

126. (New) The method of claim 125, wherein at least step (d) is carried out on a microchip.

127. (New) A method for separating DNA-containing samples, comprising:

\_\_\_\_\_ (a) providing a microchip comprised of (i) a substrate; (ii) an injection channel formed in said substrate; (iii) an electroseparation channel formed in said substrate, and disposed for fluid communication with said injection channel, and (iv) a loading reservoir formed in said substrate, and disposed for fluid communication with said injection channel;

\_\_\_\_\_ (b) placing an electrophoretic medium in said electroseparation channel;

\_\_\_\_\_ (c) placing in said reservoir (i) a DNA-containing sample including a target DNA sequence, and (ii) a peptide nucleic acid (PNA) probe labeled with a detectable moiety, said PNA probe having a sequence complementary to at least a portion of said target sequence, whereby PNA-DNA hybrids are formed;

\_\_\_\_\_ (d) applying one or more electrical potentials along said channels sufficient to cause PNA-DNA hybrids to migrate into and along said electroseparation channel; and

\_\_\_\_\_ (e) detecting for the PNA-DNA hybrids.

128. (New) The method of claim 127, wherein said injection and electroseparation channels intersect one another.

129. (New) A kit for the separation of the components of a mixed sample solution of single stranded nucleic acids and their complementary strands, and for detecting therein a selected target sequence, including:

(a) a microchip comprised of a substrate and an electroseparation channel formed in said substrate; and

(b) a peptide nucleic acid (PNA) probe labeled with a detectable moiety, said PNA probe having a sequence complementary to at least a portion of said target sequence.

130. (New) The kit of claim 129, wherein said microchip further comprises an injection channel formed in said substrate, and disposed for fluid communication with said electroseparation channel.

131. (New) The kit of claim 130, wherein said injection and electroseparation channels intersect one another.

132. (New) The kit of claim 130, wherein said microchip further comprises a loading reservoir formed in said substrate, and disposed for fluid communication with said injection channel.

133. (New) The kit of claim 129, further comprising a denaturing electrophoretic medium.

134. (New) The kit of claim 129, wherein said microchip is disposable.

## Appendix B

54. (Twice Amended) An apparatus comprising:

- d) a sample introduction zone;
- e) at least one peptide nucleic acid probe associated with a particle; and
- f) an electrophoretic separation channel in communication with said introduction zone;

wherein the peptide nucleic acid probe is disposed within the apparatus and is mobilizable at least within the separation channel.

57. (Twice Amended) An apparatus comprising:

- e) a sample introduction zone;
- f) an electrophoretic separation channel in communication with said introduction zone;
- g) at least one peptide nucleic acid probe labeled with a detectable moiety, said peptide nucleic acid probe disposed within the apparatus upstream of said separation channel and being mobilizable at least within the separation channel; and
- h) a sample incubation zone disposed in communication with the sample introduction zone and in communication with the separation channel.

58. (Twice Amended) A microchip apparatus comprising a plurality of capillary channels, each said capillary channel further comprising:

- a) a sample introduction zone;
- d) an electrophoretic separation zone in communication with said introduction zone;

- e) at least one peptide nucleic acid probe labeled with a detectable moiety, said peptide nucleic acid probe being mobilizable at least within the separation zone and disposed within the apparatus to mix upstream of the separation zone with a sample introduced in each said introduction zone, said sample comprising at least one double stranded polynucleotide, said at least one peptide nucleic acid probe having a sequence complementary to a selected target sequence suspected to be present in said at least one double stranded polynucleotide;
  - d) a nucleic acid/nucleic acid denaturing reagent permitting the formation of a peptide nucleic acid probe/nucleic acid complex when said selected target sequence is present;
  - e) a detection zone; and
  - f) said separation zone in communication with said introduction zone and said detection zone.
59. (Amended) The microchip apparatus of claim 58 wherein the separation zone of at least one of said capillary channel comprises an electrophoretic sieving medium.
60. (Amended) The microchip apparatus of claim 59 wherein the sieving medium is selected from the group consisting of polyacrylamide, agarose, polyethylene oxide, polyvinyl pyrrolidine and methylcellulose.
61. (Amended) The microchip apparatus of claim 58 wherein said denaturing reagent is selected from the group consisting of urea, formamide, and organic solvents.
62. (Twice Amended) The microchip apparatus of claim 58 wherein said denaturing reagent comprises a low ionic strength buffer.
64. (Twice Amended) The microchip apparatus of claim 58 wherein at least one of said at least one peptide nucleic acid probe comprises a charge-modifying moiety.

65. (Twice Amended) The microchip apparatus of claim 58 wherein the detectable moiety is an enzyme.
66. (Twice Amended) The microchip apparatus of claim 58 wherein said at least one peptide nucleic acid probe is associated with a particle.
67. (Twice Amended) The microchip apparatus of claim 58 wherein each said capillary channel further comprises a sample incubation zone disposed in communication with said sample introduction zone and said separation zone.
68. The microchip apparatus of claim 58 further comprising an electric power supply coupled to the microchip apparatus.
69. (Amended) The microchip apparatus of claim 68 wherein at least said sample introduction zone is in electrical connection with a high voltage and said detection zone is in electrical connection with each capillary channel and ground.
70. The microchip apparatus of claim 58 wherein the microchip is coupled to a laser-induced-fluorescence detection system.
71. (Amended) A microchip apparatus comprising a plurality of capillary channels, wherein each of said capillary channels further comprises:
  - e) a sample introduction zone;
  - f) an electrophoretic separation zone in communication with said introduction zone;
  - g) at least one peptide nucleic acid probe labeled with a detectable moiety, said peptide nucleic acid probe disposed within the apparatus upstream of the separation zone and being mobilizable at least within the separation zone; and
  - h) a detection zone; wherein said separation zone is in communication with said introduction zone and said detection zone.

75. The microchip apparatus of claim 58 wherein the detectable moiety is a colored particle.
76. The microchip apparatus of claim 58 wherein the detectable moiety is a fluorophore.
77. The microchip apparatus of claim 58 wherein the detectable moiety is a chromophore.
78. The microchip apparatus of claim 58 wherein the detectable moiety is a radioisotope.
79. The microchip apparatus of claim 58 wherein the detectable moiety is an electrochemical moiety.
80. The microchip apparatus of claim 58 wherein the detectable moiety is a chemiluminescent moiety.
81. The microchip apparatus of claim 58 wherein the detectable moiety is biotin.
82. The microchip apparatus of claim 58 wherein the detectable moiety is fluorescein.
83. (Amended) The microchip apparatus of claim 58 wherein the peptide nucleic acid probe is modified with the detectable moiety.
84. (Amended) The microchip apparatus of claim 58 wherein the detectable moiety is bound to the peptide nucleic acid probe.
85. (Amended) The microchip apparatus of claim 58 wherein the detectable moiety is associated to the peptide nucleic acid probe.
86. (Amended) The apparatus of claim 54 wherein the separation channel comprises an electrophoretic sieving medium.

87. The apparatus of claim 86 wherein the sieving medium is selected from the group consisting of polyacrylamide, agarose, polyethylene oxide, polyvinyl pyrrolidine and methylcellulose.

88. The apparatus of claim 54 further comprising a denaturing reagent selected from the group consisting of urea, formamide, and organic solvents.

89. The apparatus of claim 54 further comprising a low ionic strength buffer.

90. (Amended) The apparatus of claim 54 wherein said at least one peptide nucleic acid probe further comprises a charge-modifying moiety.

91. The apparatus of claim 54 wherein the particle is a colored particle.

92. (Amended) The apparatus of claim 54 further comprising a sample incubation zone disposed in communication with said sample introduction zone and said separation channel.

93. (Amended) The apparatus of claim 54 further comprising a sample detection zone disposed in communication with said separation channel.

94. (Amended) The apparatus of claim 57 wherein the separation channel comprises an electrophoretic sieving medium.

95. The apparatus of claim 94 wherein the sieving medium is selected from the group consisting of polyacrylamide, agarose, polyethylene oxide, polyvinyl pyrrolidine and methylcellulose.

96. The apparatus of claim 57 further comprising a denaturing reagent selected from the group consisting of urea, formamide, and organic solvents.

97. The apparatus of claim 57 further comprising a denaturing reagent comprises a low ionic strength buffer.

98. (Amended) The apparatus of claim 57 wherein said at least one peptide nucleic acid probe comprises a charge-modifying moiety.

- 99. The apparatus of claim 57 wherein the particle is a colored particle.
- 100. The apparatus of claim 57 wherein the detectable moiety is a fluorophore.
- 101. The apparatus of claim 57 wherein the detectable moiety is a chromophore.
- 102. The apparatus of claim 57 wherein the detectable moiety is a radioisotope.
- 103. The apparatus of claim 57 wherein the detectable moiety is an electrochemical moiety.
- 104. The apparatus of claim 57 wherein the detectable moiety is a chemiluminescent moiety.
- 105. The apparatus of claim 57 wherein the detectable moiety is biotin.
- 106. The apparatus of claim 57 wherein the detectable moiety is fluorescein.
- 107. (Amended) The apparatus of claim 57 wherein the peptide nucleic acid probe is modified with the detectable moiety.
- 108. (Amended) The apparatus of claim 57 wherein the detectable moiety is bound to the peptide nucleic acid probe.
- 109. (Amended) The apparatus of claim 57 wherein the detectable moiety is associated to the peptide nucleic acid probe.
- 110. The apparatus of claim 57 further comprising a sample detection zone disposed in communication with said separation channel.
- 111. (Amended) The microchip apparatus of claim 71 wherein the detectable moiety is bound to the peptide nucleic acid probe.
- 112. (Amended) The microchip apparatus of claim 71 wherein the peptide nucleic acid probe is bound to biotin.

113. (Amended) The microchip apparatus of claim 71 wherein the peptide nucleic acid probe is bound to fluorescein.

114. (Amended) The microchip apparatus of claim 71 wherein the peptide nucleic acid probe is modified with the detectable moiety.

115. (Amended) An apparatus comprising:

- a. a sample introduction zone;
- b. an electrophoretic separation channel in communication with said introduction zone;
- c. at least one peptide nucleic acid probe modified with a label, said label comprising a detectable moiety, said peptide nucleic acid probe disposed within said apparatus upstream of said separation channel and being mobilizable at least within the separation channel; and
- d. a sample incubation zone disposed in communication with the sample introduction zone and in communication with the separation channel.

116. (Amended) The apparatus of claim 115 wherein the detectable moiety is bound to the peptide nucleic acid probe.

117. (Amended) The apparatus of claim 115 wherein the peptide nucleic acid probe is bound to biotin.

118. (Amended) The apparatus of claim 115 wherein the peptide nucleic acid probe is bound to fluorescein.

119. (New) A method for separating DNA-containing samples, comprising:

- (a) providing a sample-separation device including an injection channel and an electroseparation channel, with said injection channel being disposed for fluid communication with said electroseparation channel;
- (b) placing an electrophoretic medium in said electroseparation channel;
- (c) mixing (i) a peptide nucleic acid (PNA) probe labeled with a detectable moiety and a (ii) double-stranded-DNA-containing sample under conditions permitting PNA-DNA hybrids to form, but disfavoring DNA-DNA hybrids;
- (d) introducing the mixture from step (c) into said injection channel;
- (e) applying an electrical potential along at least one of said channels sufficient to cause PNA-DNA hybrids to migrate into and along said separation channel; and
- (f) detecting for said detectable moiety.

120. (New) The method of claim 119, wherein said injection and electroseparation channels intersect one another.

121. (New) The method of claim 120, wherein said sample-separation device further comprises a reservoir, with said reservoir being disposed for fluid communication with said injection channel.

122 (New) The method of claim 121, wherein said injection channel, said electroseparation channel, and said reservoir are formed in a microchip.

123. (New) A method for separating samples, comprising:

- (a) providing an electroseparation channel;
- (b) placing an electrophoretic medium in said electroseparation channel;
- (c) mixing (i) a sample comprised of target DNA strands and DNA strands complementary to said target DNA strands, and (ii) a peptide nucleic acid (PNA) probe labeled with a detectable moiety, said PNA probe having a sequence complementary to at least a portion of said target DNA strands, whereby PNA-DNA hybrids are formed;

- (d) introducing said PNA-DNA hybrids into said electroseparation channel;
- (e) applying an electrical potential along said electroseparation channel sufficient to cause PNA-DNA hybrids to migrate along said electroseparation channel; and
- (f) detecting for said PNA-DNA hybrids.

124. (New) The method of claim 123, wherein said mixing is carried out under denaturing conditions, disfavoring DNA-DNA hybrids.

125. (New) A method for separating samples, comprising:

- (a) providing a sample comprised of double-stranded DNA;
- (b) denaturing said double-stranded DNA to form single-stranded DNA comprising target DNA strands and DNA strands complementary to said target DNA strands;
- (c) incubating the target DNA strands and DNA strands complementary to the target DNA strands with a peptide nucleic acid (PNA) probe labeled with a detectable moiety, said PNA probe having a sequence complementary to at least a portion of said target DNA strands, whereby DNA-PNA hybrids are formed;
- (d) electrophoresing said DNA-PNA hybrids; and
- (e) detecting for said PNA-DNA hybrids.

126. (New) The method of claim 125, wherein at least step (d) is carried out on a microchip.

127. (New) A method for separating DNA-containing samples, comprising:

- (a) providing a microchip comprised of (i) a substrate; (ii) an injection channel formed in said substrate; (iii) an electroseparation channel formed in said substrate, and disposed for fluid communication with said injection channel, and (iv) a loading reservoir formed in said substrate, and disposed for fluid communication with said injection channel;

- (b) placing an electrophoretic medium in said electroseparation channel;
- (c) placing in said reservoir (i) a DNA-containing sample including a target DNA sequence, and (ii) a peptide nucleic acid (PNA) probe labeled with a detectable moiety, said PNA probe having a sequence complementary to at least a portion of said target sequence, whereby PNA-DNA hybrids are formed;
- (d) applying one or more electrical potentials along said channels sufficient to cause PNA-DNA hybrids to migrate into and along said electroseparation channel; and
- (e) detecting for the PNA-DNA hybrids.

128. (New) The method of claim 127, wherein said injection and electroseparation channels intersect one another.

129. (New) A kit for the separation of the components of a mixed sample solution of single stranded nucleic acids and their complementary strands, and for detecting therein a selected target sequence, including:

- (a) a microchip comprised of a substrate and an electroseparation channel formed in said substrate; and
- (b) a peptide nucleic acid (PNA) probe labeled with a detectable moiety, said PNA probe having a sequence complementary to at least a portion of said target sequence.

130. (New) The kit of claim 129, wherein said microchip further comprises an injection channel formed in said substrate, and disposed for fluid communication with said electroseparation channel.

131. (New) The kit of claim 130, wherein said injection and electroseparation channels intersect one another.

132. (New) The kit of claim 130, wherein said microchip further comprises a loading reservoir formed in said substrate, and disposed for fluid communication with said injection channel.

133. (New) The kit of claim 129, further comprising a denaturing electrophoretic medium.

134. (New) The kit of claim 129, wherein said microchip is disposable.

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